PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CLJ/VB60452	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/011082	International filing date *(day/month/year)* 01.10.2004	Priority date *(day/month/year)* 02.10.2003
International Patent Classification (IPC) or national classification and IPC A61K39/10		
Applicant GLAXOSMITHKLINE BIOLOGICALS S.A. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10.10.2005	03.02.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Montero Lopez, B Telephone No. +31 70 340-3739

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/011082

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-155 as originally filed

   Claims, Numbers

   1-71 as originally filed

   Drawings, Sheets

   1/6-6/6 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 69, 70 with respect to industrial applicability and 71

because:

☒ the said international application, or the said claims Nos. 69, 70 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 71

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-71 partially .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-70
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-70
Industrial applicability (IA)	Yes:	Claims	1-68
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment on4.2.2005

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

No ISR has been established for Claim 71 and, consequently, no opinion will be formulated with regard to the novelty, inventive step and/or industrial applicability thereof.

Claims 69 and 70 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

1 The IPEA agrees with the lack of unity objection raised by the ISA in the SR for the following reasons:

1.1 The following separate groups of inventions have been identified in the present application.

1.1.1 Immunogenic composition comprising the B. pertussis antigen BrkA (SEQ ID NO:34); immunogenic composition comprising the gene encoding BrkA (SEQ ID NO:33). Vaccines comprising said immunogenic compositions. Method for treating or preventing Bordetella infection involving the use thereof.

1.1.2 Idem as invention 1, but referred to each one of the even-numbered sequences SEQ ID NOs:2-110 respectively, except SEQ ID NO:34.

1.2 The above 55 subject-matters are not linked so as to form a single general inventive concept for the following reasons:

1.2.1 Antigen-based vaccines against whooping cough are known in the prior art (some examples thereof can be seen in US5885587 and in Heininger et al.). Moreover, most

-if not all- the antigens of SEQ ID NOs:2-110 have been previously described (see the articles by Parkhill et al. and Fernandez et al).

1.3 In the light of the prior art the problem underlying the present application can be defined as the further provision of vaccines against whooping cough. The solutions as described and claimed can be summarized as follows:

1.4 Invention 1: Claims (1-71) - partially. Immunogenic composition comprising the B. pertussis antigen BrkA (SEQ ID NO:34); immunogenic composition comprising the gene encoding BrkA (SEQ ID NO:33). Vaccines comprising said immunogenic compositions. Method for treating or preventing Bordetella infection involving the use thereof.

1.5 Inventions 2-55: Claims (1-71) - partially. Idem as invention 1, but referred to each one of the even-numbered sequences SEQ ID NOs:2-110 respectively, except SEQ ID NO:34.

1.6 In the view of the fact that antigen-based vaccines against whooping-cough are already disclosed in the prior art, due to essential difference in the primary structure of the fifty-five solutions and due to the fact that no other technical feature can be distinguished which, in the light of the prior art, could be regarded as special technical feature common to these solutions, there is no single inventive concept underlying the plurality of claimed inventions of the present application.

1.7 Consequently, in the light of the above arguments the IPEA agrees with the objection put forward by the ISA. The present application is considered to relate to two separate inventions which lack unity in the sense of Rule 13.1 PCT.

1.8 An opinion with regard to novelty, inventive step or industrial applicability will be given only with respect to the invention first mentioned in the claims, that is, to the following subject-matter: Claims 1-71 (all of them partially): Immunogenic composition comprising the B. pertussis antigen BrkA (SEQ ID NO:34); immunogenic composition comprising the gene encoding BrkA (SEQ ID NO:33). Vaccines comprising said immunogenic compositions. Method for treating or preventing Bordetella infection involving the use thereof.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: US-A-5 885 587 (ECKHARDT ET AL) 23 March 1999 (1 999-03-23)

The document D1 is regarded as being the closest prior art and discloses antigen-based vaccines against whooping cough.

In view of the prior art cited, Claims 1 -70 appear to be novel because they refer to specific immunogenic compositions which have not been previously disclosed and, therefore, comply with the requirements of Art. 33(2) PCT.

In the light of D1, the problem to be solved consists in the provision of further antigen-based vaccines for B. pertussis infection. However, the present application discloses only effective immunogenic compositions comprising the BrkA antigen in combination with PT and FHA (see examples 12 and 13). Moreover, examples 12 and 13 state that the vaccine DTBrka alone does not provide significant protection over the control. It appears therefore that only some particular combinations of Brka with other B. pertussis antigens constitute solutions to the problem posed. Therefore, Claims 1-70 do not appear to have solved the technical problem over the whole scope of the claims.
In the light of the above reasoning, Claims 1-70 cannot be regarded as inventive in the sense of Art. 33(3) PCT.

For the assessment of the present Claims 69 and 70 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII
Certain observations on the international application

The following objections are raised on the formulation of the claims for the sake of completeness of the examination procedure according to Art. 6 PCT:

The expression "at least" adds ambiguity to the range covered by the claims.

The term "fragment" is vague term and renders the scope of the claims extremely broad.

The claims should be as concise as possible. In the present application, the number of claims does not correspond to the number of features disclosed by the invention.

The vague and imprecise statements in the description on page 3, third paragraph ("Various changes... the present disclosure"), page 86, first paragraph ("The above dosages are exemplary... within the scope of this invention") and page 95, line 3 ("The examples are illustrative, but do not limit the invention") imply that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity of the claims (Art. 6 PCT) when used to interpret them.

The expression "herein incorporated by reference" and similar ones contained in the description (like on page 87, last paragraph) imply that the patent application is not self-contained regarding the essential features of the invention, thus contravening Art. 5 PCT.